Epitomes

Important Advances in Clinical Medicine

Nuclear Medicine

The Scientific Board of the California Medical Association presents the following inventory of items of progress in nuclear medicine. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers, or scholars to stay abreast of these items of progress in nuclear medicine that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Nuclear Medicine of the California Medical Association and the summaries were prepared under its direction.

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Metaiodobenzylguanidine in the Diagnosis of Pheochromocytoma and Neuroblastoma

METAIODOBENZYLGUANIDINE (MIBG), a guanethidine derivative resembling norepinephrine in structure, was originally described by investigators at the University of Michigan; it can be labeled with iodine 123 or iodine 131. After administration, MIBG is bound to norepinephrine binding sites and subsequently stored in the neurosecretory granules of neuroectodermal cells located in the adrenal medulla, pheochromocytoma, neuroblastoma, and some other tumors of neural crest origin.

Only 25% of pheochromocytomas are diagnosed before death. The morbidity and mortality in patients with these lesions is high because of stroke, myocardial infarction, and the complications of hypertension. In unrecognized pheochromocytoma, catecholamine crisis and death can occur during the induction of anesthesia for an unrelated problem. Since 10% to 20% of pheochromocytomas are extra-adrenal or multifocal, MIBG imaging is establishing its place in the characterization of adrenal or periadrenal masses incidentally encountered in computed tomographic scans.

Imaging is usually done 24 hours after giving the patient MIBG. Images can be obtained up to 48 hours after administration with iodine 123 and even later with iodine 131. Lesion image contrast tends to improve with time, and faint normal adrenal medullary localization rarely is a problem because tumors typically show abundant uptake. Hepatic, bladder, and occasionally colonic localization normally is seen early—3 to 24 hours. Myocardial localization appears to be quantitatively related to catecholamine binding site concentration.

Reported sensitivities of MIBG imaging for the diagnosis of pheochromocytoma range between 70% and 90%. Specificities of 100% have been encountered in large series reported at both the University of Michigan and the University of California, San Francisco. Metaiodobenzylguanidine also has been useful in staging neuroblastomas and in preoperative categorizing of abdominal masses in children.

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Gallium Studies in Patients With the Acquired Immunodeficiency Syndrome (AIDS) and the AIDS-Related Complex

GALLIUM GA 67 CITRATE IMAGING has been a useful tool in evaluating patients with the acquired immunodeficiency syndrome (AIDS) or the AIDS-related complex (ARC). In identifying *Pneumocystis carinii* pneumonia, the noninvasive gallium scan, because its sensitivity is greater than 90%, is an excellent screening tool for the early detection of asymptomatic opportunistic infection with or without radiographic abnormality and as a triage device to direct the appropriate patients to bronchoscopy and bronchoalveolar lavage when tissue-specific diagnosis is needed. For example, in a group of about 30 patients studied by Kramer and colleagues, the relative sensitivity of a chest x-ray film, when compared with the gallium scan, was only 50%. Gallium scans are thus useful in identifying clinically occult *P carinii* pneumonia or may lead to a reclassification from ARC to AIDS in those patients who are asymptomatic and have a normal chest x-ray film. The pattern of gallium localization in the lungs in these patients is mainly diffuse, with intense increased uptake in both lungs, although focal localization has been noted in some patients. The focal pulmonary pattern has also been seen in patients with *Mycobacterium avium-intracellulare* and bacterial pneumonia. Other than *P carinii* pneumonia, the diffuse pattern is also seen in pulmonary infections caused by cytomegalovirus, *Cryptococcus, Toxoplasma,* and in interstitial fibrosis. Sputum retrieval, bronchial washings, or open lung biopsy must be done for a definitive diagnosis.

M avium-intracellulare is a common infection in AIDS patients. Intrathoracic regional lymph node localization of gallium 67 should suggest *M avium-intracellulare* lymphadenitis; the finding has a 90% positive predictive value. Lymphoma may present with a similar pattern, however, making tissue diagnosis imperative.

The intestine is one of the most common organs for opportunistic infections in patients with AIDS. Intense gallium

colonic uptake, especially with good bowel preparation, may suggest infection of the intestinal tract or inflammation of the intestinal mucosa. Further investigations, such as stool examination, microbiologic studies, and, if appropriate, colonoscopy with biopsy, should be done.

About 95% of the neoplasms occurring in AIDS patients are either Kaposi's sarcoma or non-Hodgkin's malignant lymphoma. Kaposi's sarcoma is common in AIDS patients and accounts for approximately 85% of cancer in male homosexuals. To date, no evidence of gallium uptake in the lesions of Kaposi's sarcoma has been reported. The gallium scan is helpful in differentiating pulmonary Kaposi's sarcoma from infection in AIDS patients with this cancer. In such patients, a normal gallium scan with an abnormal chest x-ray film increases the likelihood of pulmonary Kaposi's sarcoma.

About 4% to 10% of AIDS patients have non-Hodgkin's lymphoma. High-grade lymphomas usually have intense gallium uptake, while lower grade lymphomas usually have mild gallium uptake. The degree of uptake in the initial gallium scan appears to be inversely related to the survival times of these patients. Patients with non-Hodgkin's lymphoma frequently have extranodal involvement; gallium scanning may be superior to computed tomography scanning for staging purposes.

In conclusion, gallium scanning is clinically very useful in patients with AIDS. Because its sensitivity is greater than 90%, it can differentiate ARC from asymptomatic AIDS in the early stage of *P carinii* pneumonia. When used in patients with minimal pulmonary symptoms, gallium scans can noninvasively identify those who have infection and would benefit from bronchoscopy or lung biopsy.

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Radionuclide Evaluation of Renal Transplants

RENAL SCINTIGRAPHY has proved useful in assessing the complications of renal transplantation. Flow, morphology, and function can be evaluated without substantial risk. Complications can be divided into two categories: renal parenchymal pathology, including acute tubular necrosis (ATN) rejection, and cyclosporine nephrotoxicity; and anatomic lesions, including vascular obstruction, perinephric fluid collections, urine leak, and obstruction. The clinical findings in many of these processes are nonspecific and, in the case of rejection, may be obscured by routine immunosuppressive therapy.

The two most important radioactive nuclides in transplant imaging are technetium Tc 99m pentetic acid (DTPA) and iodohippurate sodium I 131 (Hippuran I 131). Although many abnormalities can be detected with either agent, they are in some respects complementary, and often both are used. ^{99m}Tc DTPA has better imaging properties and gives much better statistics in the usual doses, whereas iodohippurate ^{131}I is principally secreted by the tubules and is helpful when certain parenchymal lesions may be present ("polyuric" ATN or cyclosporine toxicity) with relatively normal renal flow. Both studies can be readily quantified in a variety of ways using time-activity curves and, on occasion, by sampling the plasma and urine activity. A baseline renal scan is usually done within 24 hours of transplant placement, with follow-up studies as clinically dictated.

Among the parenchymal lesions, acute tubular necrosis is characterized by relatively normal flow on the DTPA study, with very poor excretion of iodohippurate ^{131}I and poor accumulation of DTPA in the urine. As ATN resolves, the iodohippurate ^{131}I program assumes a more normal configuration. In transplant rejection, the renal perfusion is substantially diminished and renal tubular function is abnormal. A prominent collecting system ("pseudo-obstruction") may be seen in cases of rejection as well. Cyclosporine toxicity has a similar scintigraphic appearance to ATN, with diminished tubular function out of proportion to the change in renal perfusion. Many other agents have been proposed to detect rejection, including technetium Tc 99m sulfur colloid, gallium Ga 67 citrate, fibrinogen I 131, and leukocytes and platelets labeled with indium In 111. Most of these agents have proved too nonspecific to be useful, but the use of platelets labeled with ^{111}In appears promising.

Anatomic lesions are as a group best shown with ^{99m}Tc DTPA flow studies and sequential static images. Renal vascular occlusion is seen as a complete absence of renal perfusion to the kidney or the segment of kidney involved. Renal artery stenosis does not have a specific scintigraphic appearance, but the scan does show decreased perfusion in the absence of rejection by other criteria. Hematomas and lymphoceles are seen in scintigraphic studies as photopenic defects or possibly a "halo" near the transplant. Urinomas appear initially photopenic but gradually fill in with activity as tracer is excreted into the collecting system. To show the filling of a urinoma, it may be necessary to obtain postvoiding images. Occasionally obstruction of a transplanted kidney is seen that is scintigraphically similar to an obstructed collecting system in a nontransplanted kidney.

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Detection of Gastrointestinal Bleeding

ACUTE UPPER GASTROINTESTINAL BLEEDING is most often caused by gastric or duodenal ulceration, gastritis, and varices. Conservative treatment—lavage, bed rest, volume replacement, and sedation—will benefit 80% of patients with such bleeding. Lower gastrointestinal bleeding is commonly due to diverticular disease, angiodysplasia, inflammatory bowel disease, and neoplasia. Bleeding is usually intermittent.